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Application Number NDA 21-178 / 5-004

ENVIRONMENTAL ASSESSMENT and/or FONSI

INTRODUCTION

Reference is made to NDA 21-178/S-004 submitted November 30, 2001, proposing the use of Glucovance® with a thiazolidinedione when glycemic control is not obtained with Glucovance® alone. This amendment to S-004 presents a confidential assessment of Part IV: Environmental Assessment - stating that the proposed action meets the requirements for a categorical exclusion.

Due to current market conditions, the expected overall use of the active moiety, metformin hydrochloride, is not anticipated to increase in Glucophage®, Glucovance® and glipizide/metformin HCl products, above previously reported annual volumes. Confidential Appendix 1 of this amendment provides the current forecast production volumes against the forecasted production volumes for metformin hydrochloride previously reported in Part IV: Environmental Assessment, Confidential Appendix 1 of pending NDA 21-460 (glipizide and metformin HCl).

Reference is also made to a telephone conversation between Ms. E. Connolly (Bristol-Myers Squibb) and Ms. J. Weber (FDA Project Manager) on September 24, 2002, where it was agreed that Bristol-Myers Squibb would amend this supplement with a section supporting categorical exclusion from an Environmental Assessment.

PART IV. ENVIRONMENTAL ASSESSMENT

1 CATEGORICAL EXCLUSION

Metformin Hydrochloride

The subject of the proposed action meets the requirements for a categorical exclusion from submitting an environmental assessment, 21 CFR 25.31 (a). This action is not expected to increase the use of the active moiety, metformin hydrochloride, in Glucophage® and Glucovance® products, beyond annual volumes previously reported to the FDA. In addition, to Bristol-Myers Squibb Company's knowledge, no extraordinary circumstances exist [21CFR 25.15 (d)]. See also Confidential Appendix I.

Glyburide

The subject of the proposed action meets the requirements for a categorical exclusion from submitting an environmental assessment, 21 CFR 25.31 (a). To Bristol-Myers Squibb Company's knowledge, no extraordinary circumstances exist [21CFR 25.15 (d)]. The Expected Introductory Concentration to the environment is estimated to be below 1 ppb. See also Confidential Appendix 1.